

**Amendment and Response**

Serial No.: 10/549,867

Confirmation No.: 4764

Filed: September 22, 2005

For: METHODS OF PROMOTING CELL VIABILITY

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**Remarks**

The Office Action mailed March 18, 2008, has been received and reviewed. Claims 1-3, 9, 23, 27-30, 41, 44-47, 51-53, and 68-71 having been amended, claims 18-22, 31, 32, 42, 43, 48-50, and 54-65 having been canceled, without prejudice, and claims 75-80 having been added, the pending claims are claims 1-17, 23-30, 33-41, 44-47, 51-53, and 66-80. Claims 5, 6, 9-14, 23-30, 33-42, 44-54, and 69-74 being withdrawn from examination, as drawn to non-elected inventions, claims 1-4, 7, 8, 15-17, and 66-68 are presently under examination. Reconsideration and withdrawal of the rejections are respectfully requested.

Support for the amended and new claims is found throughout the specification and Applicants submit that no new matter is added thereby. For example, support for amended claims 1, 2, 23, and 27 can be found on page 8, lines 29-32 of the specification; support for amended claims 3 and 28 can be found on page 9, lines 1-3 of the specification; support for amended claims 29 and 68 can be found on page 17, lines 7-9 of the specification; support for amended claim 30 and new claim 75 can be found on page 2, line 7 of the specification; and support for amended claim 41 and new claims 77 and 78 can be found on page 18, lines 12-14 of the specification. Support for new claims 79 and 80 is found, for example, in claims 69 and 72.

**Restriction Requirement**

Applicants continue to traverse the Restriction Requirements mailed August 1, 2007, and October 30, 2007.

Applicants continue to submit that claims 1 is a linking claim, generic to the claims of Group A (drawn to the *in vitro* contacting of a cell populations with a hydrophilic bile acid) and Group B (drawn to the *in vivo* contacting of a cell population with a hydrophilic bile acid). According to MPEP 809.03, "[u]pon the indication of allowability of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise requiring all the limitations of the allowable linking claims will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104." Applicant requests the

rejoinder and examination of the claims of Group B (claims 4, 5, 44-47, and 51-53) upon the indication of the allowability of a linking claim.

Applicants submit that new claims 77 and 78 properly belong in elected Group A. The examination of claims 77 and 78 is requested.

Applicants have elected for examination claims drawn to a "method of promoting viability of a transplant cell population comprising contacting the transplant cell population with an effective amount of a compound" (see claim 1), "wherein the contacting occurs *in vitro*" (see claim 4). Applicants respectfully submit that withdrawn dependent claims 9-14 and 69-73 and new dependent claims 76, 79, and 80 all depend from elected claims 1 or 4, are thus obviously drawn to the elected method, and must be examined with elected Group A. Specifically, claims 72, 73, 76, and 77 are drawn to the method of claim 4, "***further comprising*** transplanting the cell population into a subject;" claims 69-71 and 79 are drawn to the method of claim 4, "***further comprising*** transplanting the cell population into a subject with Parkinson's disease;" and claims 9-14 are drawn to the method of claim 72, "***further comprising*** treating the subject with the compound." Thus, with dependent claims 9-14, 69-73, 76, 79, and 80 additional limitations have been added to the method currently under examination. Applicants submit that it is improper to withdraw these dependent claims, claims that include all limitations of the claims currently under examination. Withdrawing these claims from examination is denying Applicants the legal right to present dependent claims. The rejoinder and examination of claims 9-14, 69-73, 76, 79, and 80 is requested.

Applicants respectfully submit that methods claims must be analyzed for restriction based on the active method steps of the claims and submit that the withdrawal of claims 23-30 and 33-41 from examination is improper. Applicants submit that claims 23-30 and 33-41 are drawn to the currently elected method, a method of promoting viability of a transplant cell population comprising contacting the transplant cell population with an effective amount of a compound, wherein the contacting occurs *in vitro*. The rejoinder and examination of claims 23-30 and 33-41 is requested.

**The 35 U.S.C. §102 Rejection**

The Examiner has made several rejections under 35 U.S.C. 102(b). Claims 1-4, 7, 8, 15-19, 66, and 67 were rejected as being anticipated by Falasca et al.; claims 1-4, 7, 8, 15-17, and 66-68 were rejected as being anticipated by Rodrigues, et al.; and claims 1-4, 7, 8, 15-17, and 66-68 were rejected as being anticipated by Silva et al. (Journ. Of Hepatology. 2001, Vol. 34, pages 402-408). These rejections are respectfully traversed.

According to MPEP § 2131 a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Claims 1-4, 7, 8, 15-19, and 66-68 are all drawn to a "method of promoting viability of a transplant cell population comprising contacting the transplant cell population with an effective amount of a compound selected from the group consisting of ursodeoxycholic acid, a salt thereof, an analog thereof, and a combination thereof, *wherein cells of the transplant cell population are dopamine neurons or precursors thereof.*" Applicants submit that none of the teachings of Falasca et al., Rodrigues et al., or Silva et al. disclose a method "wherein cells of the transplant cell population are dopamine neurons or precursors thereof."

Thus, the disclosures of any of Falasca et al., Rodrigues et al., or Silva et al. do not set forth each and every element of claims 1-4, 7, 8, 15-19, and 66-68. Withdrawal of this rejection under 35 U.S.C. §102(b) is respectfully requested.

**The 35 U.S.C. §103 Rejection**

The Examiner rejected claims 1-4, 7-8, 15-19, and 66-68 under 35 U.S.C. 103(a) as being unpatentable over Falasca et al., Rodrigues et al., and Silva et al. This rejection is traversed.

**Deficiencies Not Corrected by Combining References**

For the reasons discussed above, Applicants submit that neither of Falasca et al., Rodrigues et al., or Silva et al. teach the claimed method. Applicants submit that the deficiencies in the teachings of any one of Falasca et al., Rodrigues et al., or Silva et al. are not

corrected by the combination of the teachings of the three references. Thus, claims 1-4, 7-8, 15-19, and 66-68 are not unpatentable under 35 U.S.C. 103(a) over Falasca et al., Rodrigues et al., and Silva et al. Withdrawal of this rejection under 35 U.S.C. §103(a) is respectfully requested.

Improper Rejection Under 35 U.S.C. §103(a)

Further, Applicants submit that this rejection under 35 U.S.C. §103(a) is improper, as the Examiner has failed to establish a proper *prima facie* case of obviousness for any of the individual claims included in this rejection. According to the MPEP, "35 U.S.C. 103 authorizes a rejection where, *to meet the claim*, it is necessary to modify a single reference or to combine it with one or more other references. After indicating that the rejection is under 35 U.S.C. 103, the examiner should set forth in the Office action:

- (A) the relevant teachings of the prior art relied upon . . . ,
- (B) the difference or differences in the claim over the applied reference(s),
- (C) the proposed modification of the applied reference(s) necessary to arrive at the claimed subject matter, and
- (D) an explanation as to why the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made" (MPEP 706.02(j) (emphasis added)).

This analysis must be articulated claim-by-claim. However, with the present rejection, the Examiner has merely provided a paragraph summarizing the teachings of Falasca et al., Rodrigues et al., and Silva et al., (page 8, Office Action mailed March 18, 2008), provided a general interpretation of the overall claimed invention (pages 8-9, Office Action mailed March 18, 2008), and concluded with the statement that "the claimed invention as a whole was clearly *prima facie* obvious" (bottom of page 9, Office Action mailed March 18, 2008). Applicants submit that the Examiner has presented only an omnibus rejection of the "claimed invention as a whole" and has failed to present a proper claim-by-claim *prima facie* case of obviousness.

"Obviousness is a question of law based on underlying factual inquiries. The factual inquiries [include] . . . [a]scertaining the differences between the claimed invention and the prior

art" (MPEP 2141). "The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious" and "[t]he examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness" (see MPEP 2142). As the Examiner has failed to articulate a proper rejection of any given claim, Applicants are not able to provide a response for any given rejected claim.

The withdrawal of this improper rejection under 35 U.S.C. §103(a) is respectfully requested. Applicants respectfully request, that if the rejection of claims is maintained in the Examiner's next Office Action, that the Examiner provide a proper, claim-by-claim *prima facie* case of obviousness. Further, Applicants submit that such an Office Action cannot properly be a Final Office Action.

#### Unexpected Results

According to MPEP 2145, "[o]ffice personnel should consider all rebuttal arguments and evidence presented by applicants," [r]ebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties," and "[e]vidence pertaining to secondary considerations **must be taken into account** whenever present" (MPEP 2145 (emphasis added)). Applicants respectfully submit that in view of the evidence of unexpected results presented by the specification, the method of claims 1-17, 23-30, 33-41, 44-47, 51-53, and 66-80 cannot be obvious.

In this regard, Applicants direct the Examiner to the evidence provided on page 16, lines 14-26 of the specification. With the present invention it has been unexpectedly discovered that contacting dopamine neurons *in vitro* with a hydrophilic bile acid "inhibit[ed] apoptosis of the transplanted cell population long enough for engraftment to take place in a subject" (page 16, lines 20-23 of the specification) and promoted viability of the cells when transplanted (page 16, lines 23-25 of the specification). It was an unexpected, surprising showing that contacting dopamine neurons *in vitro* with a hydrophilic bile acid "could be used in prompting viability of a

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transplant cell population . . . during the time frame necessary for the engraftment of the transplanted cell population" (page 16, lines 17-20 of the specification).

In view of these surprising and unexpected findings and in view of these secondary considerations of nonobviousness, Applicants submit that claims 1-17, 23-30, 33-41, 44-47, 51-53, and 66-80 are not obvious under 35 U.S.C. 103(a) over Falasca et al., Rodrigues et al., and Silva et al.

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**Summary**

It is respectfully submitted that the pending claims 1-17, 23-30, 33-41, 44-47, 51-53, and 66-80 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives at the telephone number listed below if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted

By

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**CERTIFICATE UNDER 37 CFR §1.8:**

The undersigned hereby certifies that the paper(s), as described hereinabove, are being transmitted via the U.S. Patent and Trademark Office electronic filing system in accordance with 37 CFR §1.6(a)(4) to the Patent and Trademark Office addressed to the Commissioner for Patents, Mail Stop **Amendment**, P.O. Box 1450, Alexandria, VA 22313-1450, on this 18 day of September, 2008.

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